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SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,694	BONGSO ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-76 and 79-100* is/are pending in the application.

4a) Of the above claim(s) *21-75 and 98-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *76 and 79-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/29,2/11,3/9,6/28*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Applicants' Response and Amendment, filed 6/12/06, has been entered. Claims 1-20 and 77-78 are cancelled; claims 76 and 79 are amended; claims 80-100 are newly added; claims 21-75 and 98-100 are withdrawn; claims 76 and 79-97 are under current examination.

Election/Restrictions

Applicant's election with traverse of Group IV (claims 76-79) in the reply filed on 6/12/06 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown that the claimed inventions are independent and distinct, so as to justify the restriction requirement. Applicants argue the following:

1) The conditioned media of Group IV are obtained by culturing the feeder cells of Group I, and thus, the conditioned media, of Group IV is related to the feeder cells of Group I. Further, the feeder cells of Group I and Group IV share the function of supporting the derivation and culture of ES cells in a substantially undifferentiated state.

2) The conditioned media of Group IV contains soluble factors that support the derivation and culture of ES cells in a substantially undifferentiated state, and thus, this conditioned media can be used in the method of Group II.

3) The culture system of Group III and IV are related because the culture system of Group III and the conditioned media of Group IV are specifically recognized by the inventors to be suitable for the derivation and culture of ES cells in a substantially undifferentiated state.

Applicants argue that Groups I-IV merely represent different aspects of a single invention.

Response to Arguments. This is not found persuasive because of the following:

1. The Examiner is not required to show that the inventions are both independent and distinct. Particularly, the Examiner points to MPEP ¶803 which specifically states that, "Under the statue, the claims of an application may be properly required to be restricted to one of two more claimed inventions only if they are able to support separate patents and they are either independent or distinct." Thus, the Examiner has properly found the claims to be either independent or distinct, as set forth in the Restriction requirement, mailed 5/3/06.

2. Applicants have now cancelled claims 1-20, which correspond to Group I of the Restriction requirement, mailed 5/3/06. Thus, the Examiner only addresses Applicants' comments as they apply to the pending claims. Invention II and IV are mutually exclusive and independent. The method of deriving an ES cell in a substantially undifferentiated state only requires the undifferentiated ES cells, and a cell support matrix that has soluble factors from human feeder cells, and there is no requirement for the conditioned medium of Invention IV. Inventions III and IV are shown to be distinct because they have separate uses, for example, as stated previously, that pluripotent cells, other than ES cells, can be used in the culture system of Invention III.

The requirement is still deemed proper and is therefore made FINAL.

Note. Newly submitted claims 98-100 are directed to a non-elected invention: the claims are drawn to a kit comprising conditioned medium and a cell support matrix. These claims are found to correspond to Group III of the Restriction requirement. Particularly, claim 56 recites a cell support matrix and a medium that is derived form a human feeder cell, where various claims recite the same cell types as that required by claims 98-100. Thus, these claims are found to correspond to Group III of the Restriction requirement and are withdrawn as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 21-75 and 98-100 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no

allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/12/06.

Information Disclosure Statement

Applicants' IDS, filed 3/29/04, 2/11/05, 3/9/06, 6/28/06, have been considered.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Australia (No. PR8028, PS0789, PS1812) and on September 28, 2001, February 28, 2002, and May 16, 2002, respectively. It is noted, however, that applicant has not filed a certified copy of the Australian applications as required by 35 U.S.C. 119(b).

Applicants' letter, filed 3/29/04 states Applicants' intent to file the certified copies of these Australian Patent Applications in due course, but as of the mailing date of this Office action, no certified copies have been received.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Page 39, lines 14 and 18 has sequences that do not have an appropriate sequence identifier. Applicants are required to either put the appropriate sequence identifier

Furthermore, Applicants must provide, as stated in the Notice to Comply, an substitute CRF, an substitute paper copy of the sequence listing and the

appropriate statement accompanying this submission. Appropriate correction is required in order to constitute a proper response to this Office action. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 76 and 79-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a conditioned medium for deriving and culturing an ES cell line in a substantially undifferentiated state by: obtaining a fibroblast feeder cell; culturing the fibroblast feeder cell in the presence of a medium selected from the group consisting of HES, KO, HES-HS, KO-HS, HFE, HM, HF, HF-HS and separating the medium from the cells to obtain the medium, does not reasonably provide enablement for using any feeder cell layer to condition the medium to derive and culture an ES cell line in an undifferentiated state.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention. The claims are directed to conditioned medium for deriving and culturing an ES cell line in an undifferentiated state, wherein the the medium is produced by obtaining a feeder cell layer that comprises cells selected from the group consisting of human adult cells, human fetal cells, human embryonic cells, and a combination thereof, and culturing the feeder cells in the presence of a medium selected from the group consisting of HES, KO, HES-KS, KO-HS, HFE, HM, HF, and HF-HS, and separating the medium from the cells to obtain conditioned medium. Further embodiments limit the cell types to fibroblast cells, skin cells, muscle fibroblasts, epithelial cells, and combinations thereof.

Breadth of the claims. The claims broadly encompass producing cultured medium to culture an ES cell from any species using any feeder cell layer.

Guidance of the Specification/The Existence of Working Examples. The specification teaches that human ES cells (hES) can only be maintained in an undifferentiated state on either irradiated or mitomycin-C treated mouse embryonic fibroblast feeder cells. The specification teaches methods of deriving and propagating hES cells in the absence of feeder cells. The specification teaches that cultured fibroblasts can be used in order to produce the conditioned medium (see page 21, lines 17-20), contemplating various cell lines including Detroit 551, MRC-5 or WI-38 (p. 22, lines 12-13), or other embryonic, fetal or adult skin or muscle feeder cells (p. 25, lines 1-5).

The working examples in the specification are directed to producing conditioned medium from mouse embryonic fibroblasts, human embryonic muscle, human embryonic skin, and adult human fallopian tubal fibroblast cells, (Example 1). The specification hES cells can maintain a differentiated state in the presence of MEF, adult fallopian tubal and human embryonic muscle and skin feeder fibroblast conditioned medium (p. 35, lines 5-10). The specification the human fetal muscle samples were prepared such that primary cultures of fibroblasts were established

(see p. 36, lines 24-25); the description of all the figures show that the cells used as feeder cells are all fibroblast feeder cells (see Figure legends, pages 6-7).

State of the Art/Predictability of the Art. Both the instant specification and the state of the art support that fibroblast feeder layers provide factors which are required for the maintenance of undifferentiated state. For example, Lim *et al.* [**Proteomics**, 2:1187-1203(2002), cited on Applicants' IDS, filed 6/28/06) teach that the proteome analysis of conditioned medium from mouse embryonic fibroblast feeder layers to characterize the environment that supports the growth of undifferentiated human ES cells, and to identify factors critical for their independent growth. See *Abstract.* Lim state that, "Despite many years of using mouse embryonic fibroblast cells as feeder support of human ES cells, it is still not clear what these cells for their clients. The interaction between these two cell types might take place *via* factors secreted into the medium or into extracellular matrix as well as through membrane-bound proteins." See p. 1188, 1st ¶. Lim teach that by utilizing proteomic analysis, unexpected results identify many known intracellular proteins, and that further analysis using serum-containing medium in the presence of ES cells, and using other cell types for feeder layers will be required. See p. 1203, 1st ¶, #4.

The specification clearly shows that only fibroblast cells can support the derivation and/or culture of ES cells in an undifferentiated state, as required by the claims. Although the fibroblasts taught by the specification are isolated from different sources (such as human adult muscle, fetal muscle, or embryonic muscle, for example), the working examples in the specification clearly show that the cells that are used as feeders from these sources are all fibroblast. This is supported by the art, for example, Thomson *et al.* (PNAS, 92: 7844-7848 (1995), cited as reference 7 on Applicants' IDS, filed 6/28/06) discuss the difficulties in culturing pPS in feeder free conditions. Thomson *et al.* teach the derivation of a cloned cell line from a rhesus monkey that remains undifferentiated when grown on mouse embryonic

fibroblast feeder layers, but differentiate or die in the absence of the fibroblasts (see p. 7844, *Abstract*). Particularly, Thomson *et al.* state that in the absence of the feeder layers, soluble human leukemia inhibitory factor (LIF) fails to prevent the differentiation of the cells, and that the factors that fibroblasts produce to prevent the differentiation of the cells is yet unknown (see p. 7847, 1st column, 2nd paragraph). Thomson *et al.* further state that human inner cell mass-derived cells were cultured in the absence of feeder layers failed to survive beyond 2 passages (see p. 7848, 1st paragraph). The instant specification supports Thomson's finding by teaching that an artificial growth environment, such as an extracellular matrix, and culturing the cells in a conditioned medium supports the undifferentiated growth of the hES cells. See Example I, which teaches growth of hES cells on collagen and matrigel in the presence of fibroblast-conditioned medium. However, the specification fails to provide any other teaching or guidance with regard to growth of hES in an undifferentiated state using medium conditioned by any other cell type, other than fibroblast cells.

The Amount of Experimentation Necessary. Accordingly, in view of the state of the art, with regard to the unpredictability of using any cell type, other than a fibroblast, to conditioned medium for the culture of ES cells in an undifferentiated state, the state of the art, which clearly teaches that only fibroblasts are capable of maintaining ES cells in an undifferentiated state, the working examples provided by the specification, with regard only using fibroblast-conditioned medium to maintain the ES cells in an undifferentiated state, it would have required one of skill in the art to practice undue experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 76, 79-97 are rejected under 35 U.S.C. 102(e) as being anticipated by Xu *et al.* (Pub. No. US 2002/0072117 A1, published June 13, 2002, cited as Document 1 on Applicants' IDS, filed 6/28/06).

Xu teach the culture of primate pluripotent stem (pPS) cells in the absence of feeder cells, using conditioned medium. See Abstract. They specifically teach that the cells can be human ES cells (see p. 2, ¶ 0014). The cells used to condition the medium can be any cell line, and in particular embodiments, can be a human cell line with the characteristics of fibroblast or muscle cells (p. 2, ¶ 0015). They teach compositions of proliferating pPS cells, and cell lines made from these cells (p. 2, ¶ 0017). They teach differentiating human ES cells to produce fibroblast-like cells which were then used to condition medium to culture human ES cells (p. 3, ¶0036). They specifically teach the isolation of human ES cell from blastocysts, and the isolation of the inner cell masses of blastocysts in order to establish the ES cell lines. They teach that these cells are replated on MEF feeder layers, in fresh ES medium. See p. 6, ¶0070-0071. They teach that various extracellular matrix components can be used, including Matrigel (p. 7, ¶0082). They teach that human fibroblast-like cells are especially appropriate for producing the conditioned medium (p. 9, ¶ 0109). They teach that to condition the medium, various media can be used, such as KO DMEM (p. 10 ¶0118). They teach producing human feeder cell line (p. 17, Example 7), and culturing undifferentiated ES cells in feeder free conditions using conditioned medium from the human fibroblast feeder cells (Examples 8-9), and culturing undifferentiated ES cells on human fibroblast feeder cells (Example 10).

Note that certain of the claims are directed to various sources of fibroblasts; however, neither the claims, the specification, nor the art teach any discernable difference in these fibroblasts. Thus, Xu's teaching of using any human fibroblast source for conditioning or as feeder cells, anticipate these claims, as the properties of fibroblasts are inherent to the cells.

Accordingly, Xu anticipate the claims.

Claims 76, 79-97 are rejected under 35 U.S.C. 102(e) as being anticipated by Xu (**U.S. Pat. No.**, 6,642,048 B2, published November 4, 2003, filed July 6, 2001).

Xu teach producing conditioned media for use in culturing primate pluripotent stem cells in an undifferentiated state (see Abstract). They specifically teach that the primate pluripotent stem cells can be human ES cells col. 3, lines 1-3). They teach that the cells used to condition the medium can be from a human cell line that has the characteristic of a human muscle or fibroblast cell (see p. 3, lines 4-13). They teach that the cells can be obtained any source, but include producing the cells from differentiating ES cells (col. 5, lines 43-48). They teach that the conditioned medium is prepared by culturing the cells in a medium and then harvesting the medium (col. 7, lines 56-58). They teach that media, such as KO DMEM can be used with the cells that are used to condition the medium (col. 7, lines 6-10 and 30-32).

Note that certain of the claims are directed to various sources of fibroblasts; however, neither the claims, the specification, nor the art teach any discernable difference in these fibroblasts. Accordingly, Xu anticipate the claims because they teach a conditioned medium for maintain ES cells in a medium that has been conditioned with a human feeder layer, and separating the medium from the cells to obtain the medium.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 76, 79-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bodnar *et al.* (WO 99/20740, published April 29, 1999, Document #3, on Applicants' IDS, filed 6/28/06) when taken with Bongso *et al.* (**Hum. Reprod.**, 9(11): 2110-2117 (1994), cited on Applicants' IDS, filed 3/2904).

The claims are directed to a conditioned medium for deriving and culturing an ES cell line in a substantially undifferentiated state, prepared by obtaining a feeder cell layer, which supports the derivation and/or culture of ES ells in an undifferentiated state, wherein the feeder cell layer comprises cells selected from the group consisting of human adult cells, human fetal cells, human embryonic cells, and a combination thereof, and culturing the feeder cells in the presence of a medium selected from the group consisting of HES, KO, HES-HS, KO-HS, HFE, HM, HF, HF-HS and separating the medium from the cells to obtain the medium.

The claims are product by process claims. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Bodnar *et al.* teach the growth of primate-derived primordial stem cells by culturing the cells in a nutrient medium, and a substrate consisting of feeder cells, and an extracellular matrix component. See Abstract. They teach that primordial stem cells can be isolated from any source, including primates, and humans. The primordial stem cells that are contemplated by Bodnar include ES cells, as they teach that these cells are "totipotent" (see p. 1, lines 14-16, and p. 6, lines 7-9, section 3.1.10). The culture medium is effective to support the growth of the primordial stem cells (p. 2, lines 21-30) and can include various growth factors, that can be determined in order to maintain the primordial stem cells in an undifferentiated state (p. 4, lines 9-20). They teach that a conditioned medium can be made by supplementing with soluble factors derived from feeder cells (p. 5, lines 1-3 section 3.1.2). The cells can either be grown in the culture medium with feeder

cells, or an extracellular matrix produced from the feeder cells (p. 7, lines 21-28). They teach that the fibroblast feeder cells can be from mouse, or other species (see p. 10, lines 1-2). They teach the isolation of the primate primordial stem cells (p. 11, section 3.2.2). They teach that the methods can be used to produce new primate stem cell lines (p. 14, section 3.4). In particular, they teach that conditioned medium was made, using mouse embryonic fibroblasts in ES cell medium. They teach the growth of primate-derived primordial stem cells on a fibroblast feeder layer and conditioned medium. See p. 19, section 4.1. They teach the growth of rhesus-derived ES cells without a feeder, using conditioned medium and a fibroblast matrix. See p. 2, section 4.2.

Bodnar *et al.* do not specifically teach using a human feeder cell for conditioning the media. However, prior to the time the claimed invention was made, Bongso *et al.* teach the development of human embryos to blastocyst stage on human tubal epithelial monolayers, and then after blastocyst formation, the hatched ICM and trophoblast were allowed to attach to the feeder monolayer. They further teach that healthy ICM lumps could be separated and grown *in vitro* (see Abstract). They teach that the ICM, if isolated, contain ES cells (see page 2110, 1st).

Accordingly, in view of the combined teachings of Bodnar and Bongso, it would have been obvious for one of skill in the art to modify the techniques to produce conditioned medium, as taught by Bodnar, to use a human cell line, as taught by Bongso, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make this modification, because Bongso clearly show that ES cells can be grown on human feeder layers, and provide motivation in stating that, "A feeder cell type similar to the species of the embryo may be more ideal than that of a heterologous species." See page 2116, 1st column, 2nd paragraph.

Note: the claims are directed to various sources of fibroblasts (claims 82-97). However, neither the claims, the specification, nor the art teach any discernable

difference in these fibroblasts, and the properties of fibroblasts, such as the ability to maintain cells in an undifferentiated state, are inherent to the cells. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

thaian ton

Thaian N. Ton
Patent Examiner
Group 1632

Application No.: 10/811,694

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a Sequence Listing as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the Sequence Listing in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the Sequence Listing in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up Raw Sequence Listing.

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the Sequence Listing is not the same as the computer readable from of the □Sequence Listing as required by 37 C.F.R. 1.821(e).

☒ 7. Other: page 39, lines 14 and 18 have sequences without an appropriate sequence identifier.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the Sequence Listing.

☒ An initial or substitute paper copy of the Sequence Listing, as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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